**Effect of Different Excipients on Retarding Salbutamol Sulphate Release from Floating Effervescent Tablets**

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**ABSTRACT**

The objective of this work was to prepare and evaluate the effects of various concentrations of excipients on Salbutamol sulphate release from floating effervescent tablets. Salbutamol sulphate undergoes extensive first-pass metabolism and has a half-life about 4.5 hrs. The reported oral bioavailability is ~ 40 %and thus requires frequent administrations by oral route. It has a site-specific absorption in stomach and upper part of small intestine. Therefore, it is useful to prepare floating effervescent tablets of Salbutamol sulphate. This will provide a sustained release of the drug, less doses per day and will increase the patient commitment to the treatment. The materials used were Salbutamol sulphate, Sodium bicarbonate, Aerosil 200, Avicel 102, Magnesium stearate, HPMC K100M, HPMC K15M and Xanthan gum. All the formulas were subjected to DSC (Differential Scanning Calorimetry), hardness test, friability test, content uniformity, floating lag time test and dissolution test. Xanthan gum 30% was observed to give extended release floating effervescent tablets of salbutamol sulphate for 24 hours, the percent of drug released was 82.86% after 24 hours while HPMC K100M 60% formula and HPMC K15M 60% formula showed close extended release for 12 hours, the drug released from HPMC K100M and HPMC K15M 60% formulas after 12 hours was 81.06%, 83.32% respectively.

**Keywords:** Salbutamol sulphate, Floating tablets, HPMC, Xanthan gum, Extended release.

**INTRODUCTION**

Asthma is a common respiratory disease that affects the children and adults. The drugs of choice for mild asthma—that is, in patients showing only occasional, intermittent symptoms are β2 adrenergic agonists. Direct-actingβ2 agonists are potent bronchodilators that relax airway smooth muscle. There are two kinds of β2 adrenergic agonists; short acting drugs i.e. Salbutamol (Albuterol), Perbuterol, and Terbutaline, and long acting drugs i.e. Salmeterol, Formoterol.

Salbutamol sulfate (SS), a BCS class I drug, exists commercially as sulphate salt in 2 or 4 mg tablets, 4 or 8 mg capsules, 2 mg per 5 ml oral syrup, 500 µg/ml injections, 1 mg/ml solutions for intravenous infusion must be diluted before use, 100 µg/ml aerosol inhalation, 100 or 200 µg/puff inhalation powder and 1 or 2 mg/ml nebulizer solution. The oral dose of salbutamol sulphate for adults is 4 mg 3-4 times per day. The individual dose mustn’t exceed 8 mg.

Asthma being a chronic disease, and as most of the patients suffer from nocturnal attacks, there is need for drug delivery systems which maintain therapeutic concentrations for long duration. Therefore, it is useful to make a drug delivery system which remains for a long time in the stomach instead of the conventional forms.

FDDS or hydrodynamically balanced systems have a bulk density lower than gastric fluid and thus remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. Those systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability.

FDDS is suitable for drugs with an absorption window in the stomach or the upper small intestine, for drugs which act locally in the stomach and for drugs that are poorly soluble or unstable in the intestinal fluid.

Such systems cannot be used in the case of drugs like aspirin and other nonsteroidal anti-inflammatory drugs like aspirin and other nonsteroidal anti-inflammatory drugs that induce gastric lesions or for drugs that are unstable in the acidic environment of stomach. Many times it is difficult to incorporate a drug in such gastric retention systems. The retention of these systems depends on many factors such as gastric motility, pH, and presence of food. It is not easy to design and fabricate a system that can overcome all these difficulties.

**MATERIALS AND METHODS**

**Materials**

- Salbutamol sulphate (Litaka Pharmaceutical Ltd. Pune, India)
- Sodium bicarbonate (Nitika, India)
- Aerosil 200 (BASF, Germany)
- Avicel PH 102 (FMC International, Ireland)
- Magnesium stearate (Nitika, India)
- HPMC K100M (Colorcon Asia Pvt. Ltd. Goa, India)
- HPMC K15M (Colorcon Asia Pvt. Ltd. Goa, India)
- Xanthan gum (Loba Chemicals, Mumbai)
Instruments

- USP dissolution testing apparatus 2 (Erweka, tupe DT 800, Germany)
- Spectrophotometer (Shimadzu UV-1601 UV/Vis double beam)
- DSC apparatus (METTLER TOLEDO, OH, USA)
- Electronic balance 0.01g (Sartorius GP 2102, Germany)
- Electronic balance 0.001g (Shimadzu auw220d dual-range semi-micro)
- Microprocessor pH Meter (HANNA instruments pH 211, USA)
- Pharmacopoeial sieves (CISA, UK)
- Compression machine (Erweka EK-0, Motor Drive AR 402, Heusenstamm, Germany)
- Hardness and diameter tester (Erweka TBH 300S, GmbH, Germany)
- Friability tester (ErwekaTAR20, GmbH Roche, Germany)
- Nylon filter 0.45 micron (Whatman, Germany)

Methods

Drug scanning

Salbutamol sulphate (SS) dissolved in HCL (pH= 1) was scanned by spectrophotometer in the Visible spectrum and UV spectrum to determine the maximum absorption wavelength. Two concentrations of SS solution10 µg/ml and 80 µg/ml were scanned at wavelength 200- 400 nm. Three absorption peaks were observed at 204 nm, 224 nm and 276 nm. Wavelength 224 nm was considered more sensitive to the small concentrations than the USP wavelength 276 nm and it is used in other studies about SS11,12 Therefore, wavelength 224 nm was used to measure the samples withdrawn at the dissolution test, while the 276 nm wavelength was used to measure the concentrations in the content assay test.

Floating tablets preparation

Nine formulas were prepared (according to table 1) by using Salbutamol sulphate and other excipients. These tablets were prepared by direct compression (DC). Particles dimensions were 200-300 micron. Amounts were weighed accurately. Salbutamol sulphate was blended with Aerosol to improve drug flow ability, half amount of magnesium stearate to delay drug release (by covering the particles of the active ingredient) and other excipients in order. At last, the rest amount of magnesium stearate was added as a lubricant and blended for 5 minutes. The same order in mixing all materials was taken in account in preparing all formulas. Materials mixture was compressed by 10 mm standard concave punches plain on both sides. The maximum force was applied to get the maximum hardness of the tablets and therefore delaying the drug release as possible.

Drug-polymer interaction study

Compatibility of the drug with excipients was determined by Differential scanning calorimeter (DSC). Thermograms of the samples that contain Salbutamol sulphate powder and physical mixture of SS and different polymers individually were studied using a DSC apparatus (METTLER TOLEDO, OH, USA) at a scanning speed of 10°C/min in the temperature range of 25-300°C in crimped aluminum pans under nitrogen gas flow.

The percentage of the mixture was chosen depending on the percent of drug to the excipient in the formulas prepared. The samples studied were:

- SS
- Xanthan gum
- HPMC K15M
- HPMC K100M
- SS: Xanthan gum (1/5)
- SS: HPMC K15M (1/10)
- SS: HPMC K100M (1/10)

Testing the mixture of powders prepared for compression

The mixture prepared for compression was tested by measuring angle of repose, bulk density, tapped density, Carr’s index, and Hausner’s ratio. These aspects were measured to determine the mixture flow ability inside the compression machine.

Evaluation of physical parameters of matrix tablets

The prepared matrix tablets were evaluated as per standard procedure according to USP13 for hardness and diameter (n=6) and friability (n=19). Hardness and diameter of the tablets was determined using hardness tester (ERWEKA TBH 300S, GmbH, Germany) and friability was conducted using an ERWEKA Friabilator (ERWEKA TAR20- GmbH Roche, Germany) at speed of 25 rpm for 4 min. Means and standard deviations were calculated for each formulation.

Assay of salbutamol sulphate in matrix tablets (Content uniformity)14

Twenty five tablets were weighed and average weight was calculated, crushed to fine powder. The powder equivalent to 100 mg of Salbutamol was transferred in 100 ml volumetric flask and dissolved in 0.1N HCl by shaking. Frequent shaking given and volume was made up to 100ml mark with 0.1N HCL to get final concentration of 1mg/ml. The solution was then filtered through Whatman filter paper. This filtrate was diluted suitably with 0.1N HCL to get the solution of 100µg/ml concentration. The absorbance of this solution was measured at wavelength 276 nm and amount of SS was...
calculated from the standard curve plotted between concentrations and absorbance at wavelength 276 nm. The readings were taken in triplicate and the results were averaged. A blank solution containing all the components, except for the drug, was also prepared. No other assay methods were considered necessary, since no interference was observed at 276 nm. Means and standard deviations of the content were calculated for each formulation.

**Evaluation of floating lag time**\(^{15}\)

The in vitro buoyancy was determined by floating lag time, as per the method described by Rosa et al. The tablets were placed in a 100 ml beaker containing 0.1N HCl. The time required for the tablet to rise to the surface was determined as floating lag time.

**In Vitro Dissolution Studies**\(^{15}\)

The release rate of Salbutamol sulphate from floating tablets (n = 6) was determined using Dissolution Testing Apparatus 2 (paddle method). The dissolution test was performed using 900 mL of 0.1N HCl at 37 ± 0.5°C and 75 rpm. A sample (10 mL) of the solution was withdrawn from the dissolution apparatus after (1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 16, 20, 24) hours, and the samples were replaced with fresh dissolution medium. The samples were filtered through Whatman filter paper and the absorbance of these solutions was measured at 224.0 nm. The quantities released were calculated from the standard curve plotted between concentrations and absorbance at wavelength 224 nm. The averages were calculated and the dissolution profiles were plotted i.e. the relations between Q% and time.

Statistical study was applied by using t-student test to determine if there is a significant difference between HPMC K100M, HPMC K15M and Xanthan gum. If t-stat calculated is smaller than t-critical, there is no significant difference between the two formulas studied and vice-versa.

**Table 1: Formulas prepared of Salbutamol sulphate**

<table>
<thead>
<tr>
<th>Test</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
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</thead>
<tbody>
<tr>
<td>Salbutamol sulphate</td>
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<td>20</td>
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<td>20</td>
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<tr>
<td>HPMC K100M</td>
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<td>210</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>HPMC K15M</td>
<td>0</td>
<td>0</td>
<td>140</td>
<td>175</td>
<td>210</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Xanthan gum</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>35</td>
<td>70</td>
<td>105</td>
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<td>Na bicarbonate</td>
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<td>80</td>
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<td>Aerosil 200</td>
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<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Avicel 102</td>
<td>71</td>
<td>36</td>
<td>71</td>
<td>36</td>
<td>1</td>
<td>176</td>
<td>141</td>
<td>106</td>
<td>106</td>
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<tr>
<td>Final weight</td>
<td>350</td>
<td>350</td>
<td>350</td>
<td>350</td>
<td>350</td>
<td>350</td>
<td>350</td>
<td>350</td>
<td>350</td>
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</table>

**Table 2: Results of the mixture prepared for compression**

<table>
<thead>
<tr>
<th>Angle of repose</th>
<th>Bulk density</th>
<th>Tapped density</th>
<th>Carr’s index</th>
<th>Hausner’s ratio</th>
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<tbody>
<tr>
<td>F 1</td>
<td>24.30±0.57</td>
<td>0.44±0.0057</td>
<td>0.49±0.0023</td>
<td>9.77</td>
</tr>
<tr>
<td>F 2</td>
<td>24.50±0.50</td>
<td>0.43±0.0028</td>
<td>0.48±0.0017</td>
<td>10.20</td>
</tr>
<tr>
<td>F 3</td>
<td>26.60±0.36</td>
<td>0.44±0.0028</td>
<td>0.49±0.0028</td>
<td>10.36</td>
</tr>
<tr>
<td>F 4</td>
<td>26.50±0.50</td>
<td>0.31±0.0050</td>
<td>0.35±0.0023</td>
<td>10.54</td>
</tr>
<tr>
<td>F 5</td>
<td>26.00±1.00</td>
<td>0.38±0.0034</td>
<td>0.42±0.0011</td>
<td>10.11</td>
</tr>
<tr>
<td>F 6</td>
<td>25.53±0.57</td>
<td>0.32±0.0011</td>
<td>0.35±0.0020</td>
<td>10.05</td>
</tr>
<tr>
<td>F 7</td>
<td>25.20±0.26</td>
<td>0.42±0.0011</td>
<td>0.46±0.0026</td>
<td>9.40</td>
</tr>
<tr>
<td>F 8</td>
<td>24.43±0.51</td>
<td>0.45±0.0017</td>
<td>0.49±0.0026</td>
<td>9.25</td>
</tr>
<tr>
<td>F 9</td>
<td>24.83±0.28</td>
<td>0.44±0.0026</td>
<td>0.49±0.0051</td>
<td>9.79</td>
</tr>
</tbody>
</table>

**Table 3: Physical parameters results**

<table>
<thead>
<tr>
<th>Test</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
<th>F9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hardness (kg/cm²)</td>
<td>6.43±0.404</td>
<td>6.60±0.201</td>
<td>7.36±0.052</td>
<td>4.63±0.057</td>
<td>5.40±0.10</td>
<td>6.56±0.050</td>
<td>2.23±0.251</td>
<td>2.46±0.152</td>
<td>3.06±0.057</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>0.15</td>
<td>0.11</td>
<td>0.10</td>
<td>0.12</td>
<td>0.11</td>
<td>0.11</td>
<td>0.18</td>
<td>0.15</td>
<td>0.12</td>
</tr>
<tr>
<td>Content uniformity (%)</td>
<td>95.1±1.153</td>
<td>95.16±2.254</td>
<td>97.93±1.656</td>
<td>106.66±1.527</td>
<td>105.33±2.081</td>
<td>98.93±2.020</td>
<td>96.50±1.802</td>
<td>102.66±1.527</td>
<td>103.33±2.516</td>
</tr>
<tr>
<td>Floating lag time (sec.)</td>
<td>12.0±1.5</td>
<td>19.66±0.57</td>
<td>53.33±1.52</td>
<td>10.66±0.5</td>
<td>13.5±0.5</td>
<td>49.66±0.57</td>
<td>8.33±0.26</td>
<td>14.83±1.75</td>
<td>59.66±1.52</td>
</tr>
<tr>
<td>Diameter (mm)</td>
<td>10.23±0.21</td>
<td>10.21±0.24</td>
<td>10.20±0.22</td>
<td>10.22±0.23</td>
<td>10.19±0.22</td>
<td>10.21±0.19</td>
<td>10.18±0.24</td>
<td>10.17±0.22</td>
<td>10.19±0.25</td>
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</table>
**Drug Release Kinetics Studies**

Many models have been developed to describe the process of drug release from matrices. To study the release kinetics of SS from matrix tablets, the release data of the best three formulas were fitted to five kinetic models equations to find the equation with the best fit according to higher value of correlation coefficient (R²).

Zero-order: $Q_t = k_0 \cdot t$

First – order $\ln (100-Q_0) = \ln 100 - k_1 \cdot t$

Higuchi: $Q_t = k_{hc} \cdot t^{1/2}$

Hixson-Crowell: $Q_t = k_{hc} \cdot t^{1/3}$

Where $Q_t$ is the amount of drug release at time $t$, $Q_0$ is the initial amount of the drug in tablet and $k_0$, $k_1$, $k_{hc}$ and $k_{hc}$ are the rate constants of zero-order, first-order, Higuchi and Hixson-Crowell model, respectively. Later, in order to better characterize the drug release mechanisms for the polymeric matrix studied, the Korsmeyer-Peppas semi empirical model was applied.

$$Q_t/Q_{∞} = K_{pp} \cdot t^n$$

Where $Q_t/Q_{∞}$ is the fraction of drug released at time $t$, $K_{pp}$ a constant compromising the structural and geometric characteristics of the device (characteristic of the drug/polymer system), and $n$, the release exponent, which is indicative of the mechanism of the drug release.

For the case of cylindrical geometries such as tablets, $n=0.45$ indicates a classical Fickian diffusion controlling drug release (Case I), $n=0.89$ indicates a zero order (Case II and swelling of the polymer is controlling the drug release) release kinetics, $n=0.89$ indicate a super Case II transport and $0.45<n<0.89$ indicates a non-Fickian (anomalous transport) release kinetics which as both phenomena (drug diffusion and polymer swelling in the matrix).

To characterize the drug release rate, the mean dissolution time (MDT) is applied. MDT is determined as the sum of the individual periods of time during which a specific fraction of the total dose is released. MDT can be calculated according to the following equation.

$$MDT = \frac{\sum_{j=1}^{n} \Delta M_j}{\sum_{j=1}^{n} t_j}$$

Where $j$ is the sample number, $n$ is the number of dissolution sample times, $t_j$ is the time at midpoint between $t_j$ and $t_{j+1}$ (easily calculated with the expression $(t_j + t_{j+1})/2$ and $\Delta M$ is the additional amount of drug dissolved between $t_j$ and $t_{j+1}$. A higher value of MDT parameter indicates a higher drug retarding ability of the polymer in formulation and vice-versa.

**RESULTS AND DISCUSSION**

**Differential Scanning Calorimetry (DSC)**

The DSC thermogram of pure SS showed a crystal nature of the drug and exhibited an initially flat profile, followed by a single sharp endothermic peak at 201.98 °C corresponding to the decomposition of salbutamol sulphate molecule (Figure 1, a). Xanthan gum (Figure 1, b) and HPMC K15M (Figure 1, c) polymers showed an endothermic peak at 87.06 and 75.06 °C, respectively. HPMC K100M showed two endothermic peaks at 74.88 and 174.94 °C (figure 1, d).

The thermogram of binary SS and Xanthan gum physical mixture (1:5) showed two endothermic peaks (Figure 1, e), the first peak at 83.98 °C belongs to Xanthan gum and the second peak at 200.91 °C is close to SS decomposition point. The thermogram of binary SS and HPMC K15M polymer physical mixture (1:10) showed two endothermic peaks at 71.91 and 200.75°C corresponding to HPMC K15M and SS endothermic peaks, respectively (Figure 1, f). The thermogram of binary SS and HPMC K100M polymer physical mixtures (1:10) showed three endothermic peaks at 71.58, 174.64 and 200.94 °C. The first two peaks were corresponding to HPMC K100M endothermic peaks and the third to SS endothermic peak (Figure 1, g).

Drug and polymers displayed their characteristic individual melting trends without any appreciable deviation which shows that there is no interaction between drug and polymers in the formulated tablets.

**Figure 1: DSC thermograms of SS (a), Xanthan gum (b), HPMC K15M (c), HPMC K100M (d), SS and Xanthan gum mixture (e), SS and HPMC K15M (f), SS and HPMC K100M (g)**

**Mixture of powders prepared for compression**

Table 2 demonstrates the results got from testing the mixture of powders. All formulas showed acceptable results. Angles of repose of all formulas were in range 24.30-26.50 (less than 40 degree). Carr’s index was in range 9.25-10.54 (in the range 5-15). Hausner’s ratio was in range 1.101-1.117 (less than 1.25). These results refer to a good flow ability and therefore uniformity in tablets weight and content in all formulas.

**Physical parameters of matrix tablets**

The tablet hardness, diameter, friability for each extended release (ER) formulation are showed in Table 3.
HPMC K100M tablets showed the highest hardness within the range 6.43 ± 0.404 to 7.36 ± 0.052 kg/cm², while HPMC K15M tablets showed hardness within the range 4.63 ± 0.057 to 5.65 ± 0.050 kg/cm². Xanthan gum tablets showed the smallest values of hardness, although the high compression pressure applied to them, in the range 2.23 ± 0.251 to 3.06 ± 0.057 kg/cm². However, hardness always remained within the highest values possible to get to give good handling properties without breakage or excessive friability problems. It was obvious that tablet hardness increases as the matrix excipient increases. Friability results were in range 0.10-0.18% so that the tablet friability was found to be within Pharmacopoeial limits i.e. less than 1%. Tablets diameters were in range 10.17±0.22 to 10.23±0.21mm

**Uniformity of content**

All formulations have content of drug between 95.1±1.153 to 106.66±1.527 % (Table 3). The tablets content were found to be within Pharmacopoeial limits (from 90 to 110 %). Therefore, drug content uniformity indicated the presence of an acceptable amount of drug in the prepared formulations.

**Floating lag time**

As table 3 shows, floating lag time of all formulations was in range 8.33±2.08 to 59.66±1.52 seconds. It was obvious that floating lag time increases as the matrix excipient increases in the tablet. Therefore, floating lag time in xanthan gum 30% tablets, HPMC K100M 60% tablets and HPMC K15M 60% tablets were 59.66±1.52, 53.33±0.57 and 49.66±0.57 seconds, respectively, while other formulas showed a faster floating as the matrix excipient decreases in the tablet.

**In vitro dissolution studies**

Figures 2, 3, 4 show the effect of the percentage of matrix excipient (HPMC K100M 40%, 50%, 60%), (HPMC K15M 40%, 50%, 60%) and (Xanthan gum 10%, 20%, 30%), respectively, on the release of Salbutamol sulphate from the tablet. The dissolution test was stopped when 80% at least of Salbutamol sulphate was released from the tablet.

HPMC K100M 40%, 50%, 60% released at the first hour 27.913, 21.635, 15.684%, respectively, while HPMC K15M 40%, 50%, 60% released at the first hour 70.875, 48.293, 21.065%, respectively. HPMC K100M 60% and HPMC K15M 60% gave close results after 12 hours. The percentage of drug released after 12 hours from HPMC K100M 60% and HPMC K15M 60% tablets were 81.06% and 83.32%, respectively, Xanthan gum showed at the highest concentration the best results of all formulas. Xanthan gum 30% released at the first hour 11.935% and after 24 hours 82.86%, while other concentrations 10% and 20% gave a fast release of Salbutamol sulphate without showing any sustained release effect.
T-student where calculated also to determine if there is a significant difference between HPMC K100M 60% and Xanthan gum 30% in different times. Between the 1st and the 8th hour there was no significant difference between HPMC K100M 60% and Xanthan gum 30% (t-stat= 0.5372, t-critical= 2.2099). When t-test was calculated from the 8th hour to the 12th hour, it showed that there is a significant difference between HPMC K100M 60% and Xanthan gum 30% at these times (t-test= 4.895, t-critical= 2.5705). Therefore, Xanthan gum is better than HPMC K100M in retarding drug release from the tablet after the 8th hour.

**Release Kinetics**

In order to describe the kinetics of drug release from controlled release matrix tablets and to analyze correlation Coefficient ($R^2$) values of all series (Table 4), it was found that HPMC K100M 60%, HPMC K15M 60%, Xanthan gum 30% matrix tablets formulations showed a good fit into the Higuchi kinetic model ($R^2 = 0.987, 0.999, 0.989$, respectively). This refer to that Salbutamol sulphate releasing model from HPMC K100M, HPMC K15M, Xanthan gum matrix tablets is close to Higuchi kinetic model.

From Korsmeyer-Peppas model the values of release exponent (n) in HPMC K100M 60%, HPMC K15M 60%, Xanthan gum 30% matrix tablets (n= 0.714, 0.553, 0.580) indicating anomalous or non Fickian transport. The values of (n) and (k) were found to vary with type and concentration of polymer.

**Table 4: In-vitro release kinetic parameters of Salbutamol sulphate from the best three sustained matrix tablets**

<table>
<thead>
<tr>
<th>Formula</th>
<th>$t_{50%}$ (h)</th>
<th>$t_{80%}$ (h)</th>
<th>MDT (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F 1</td>
<td>3.0864</td>
<td>6.3174</td>
<td>2.875993</td>
</tr>
<tr>
<td>F 2</td>
<td>4.5518</td>
<td>8.9168</td>
<td>3.970797</td>
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<td>F 3</td>
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<td>F 4</td>
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</tr>
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<td>1.0398</td>
<td>8.9478</td>
<td>2.105412</td>
</tr>
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<td>F 6</td>
<td>4.6682</td>
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<td>F 7</td>
<td>0.504</td>
<td>2.854</td>
<td>0.583469</td>
</tr>
<tr>
<td>F 8</td>
<td>0.5529</td>
<td>2.01</td>
<td>0.708251</td>
</tr>
<tr>
<td>F 9</td>
<td>7.4999</td>
<td>20.5499</td>
<td>7.232238</td>
</tr>
</tbody>
</table>

Mean dissolution time (MDT) value is used to characterize drug release rate from a dosage form and indicates the drug release retarding efficiency of a polymer used within a formulation. Tablets prepared with Xanthan gum 30% showed highest MDT value (7.232 hours), while tablets prepared of Xanthan gum 10% showed the lowest MDT value (0.583 hours) as shown in Figure 5. This large difference between the highest and the lowest percentage can be attributed to the colloidal structure which is formed between particles in the highest concentration and this structure delay obviously the drug release while in the lowest concentration, the particles are distributed in long distances and therefore, no colloidal structure is formed. For HPMC K100M 40%, 50%, 60% tablets, MDT values were 2.876, 3.970, 4.645 hours, respectively. And for HPMC K15M 40%, 50%, 60% tablets, MDT values were 0.682, 2.105, 3.983 hours, respectively.

**CONCLUSION**

This study proved that HPMC K100M, HPMC K15M and Xanthan gum can be used to delay Salbutamol sulphate release from its tablets in certain concentrations. The best results were obtained from Xanthan gum 30% tablets. These tablets showed a sustained release of Salbutamol sulphate exceed 24 hours, while Xanthan gum 10%, 20% tablets didn’t show any role in delaying the drug release. This difference in effect on the drug release can be attributed to the coherent colloidal structure formed Xanthan gum 30% in acidic medium HCL 0.1N comparing to the incoherent structure of the percentage 10% and 20% of this gum. HPMC K100M and HPMC K15M.
showed close results after 12 hours with no significant difference in releasing Salbutamol sulphate.

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